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PRIORITY LETTER

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Commissioner for Patents
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Pursuant to the provisions of 35 U.S.C. 119, enclosed is/are a certified copy of the following priority document(s).

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PA 2000 00759	5/8/2000	Denmark

In support of Applicant's priority claim, please enter this document into the file.

Respectfully submitted,

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Patent- og Varemærkestyrelsen
Økonomi- og Erhvervsministeriet

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Åse Damm

PATENT- OG VAREMÆRKESTYRELSEN

METHOD FOR PERFORMING CHEMICAL REACTIONS AND A KIT THEREFOR

FIELD OF THE INVENTION

The present invention relates to a method for selecting reaction parameters for a chemical reaction and to a method for conducting a chemical reaction in an apparatus which provides energy for the chemical reaction, where a particular advantage is the use of predetermined reaction parameters corresponding to similar chemical reactions. The present invention also relates to kits for performing said method. It is believed that the methods and the kits according to the present invention will have a broad field of application, e.g. for the organic chemist, in the analytical and diagnostic fields, in the "large scale" production of complex chemical compounds, etc.

BACKGROUND OF THE INVENTION

Automated synthesis and diagnostic processes has met increasing interest in the last decades. In view of the need for standardised processes yielding product and results of uniform quality, a number of useful apparatuses and methods for synthesis and diagnostic processes have been developed. A wide range of apparatuses are commercially available, especially in the field of peptide and oligonucleotide synthesis where standardised synthetic steps can be described in great detail.

Another field of great interest is the field of development of novel organic compounds, e.g. novel drug candidates. Some of the major obstacles for an organic chemist today are the time consumed, the complexity, and the search for efficient routes in organic synthesis. As an example, the average performance some ten years ago was around 25-50 complete substances per chemist a year in the pharmaceutical industry, resulting in an equal amount of new chemical entities as potential new drug candidates. Today the figure is close to 100's per year and will soon be expected to be in the region of 1000's per year per day.

Thus, the challenges for the pharmaceutical industry and the organic chemist include identification of ways of reducing time in the drug development, identification of ways of creating chemical diversity, development of new synthesis routes and

reintroduction of old "impossible" synthetic routes. Also, it is a constant challenge to reach classes of totally new chemical entities.

Microwaves assisted chemistry offers a way of providing solutions to at least some of the above problems, namely by

- speeding up the reaction time with orders of magnitude,
- improving the yield of chemical reactions,
- offering higher purity of the resulting product due to rapid heating and thereby reducing impurities from side reactions, and
- making reactions which were not considered possible with conventional thermal heating possible.

However, it has often been considered difficult to select optimal conditions when using microwave ovens in that suitable reaction conditions often are found within a very narrow "window". In particular, it is usually considered quite difficult to determine the most suitable combination of process parameters, e.g. applied power, time, solvent, etc.

Although the organic chemist has knowledge about a wide variety of chemical reaction types, he will, if possible, tend to select familiar reaction types even when totally new chemical entities are to be synthesised. Thus, for the organic chemist, it would be desirable if he could gain access to "novel" reaction types associated with reagents unfamiliar to him in a easy manner. Preferably, the automated synthesis of novel drug candidates and other complex chemical entities should not be limited to "chemistries" developed by the organic chemist operating the apparatus or to a very limited number of standard protocols provided by the supplier as, e.g., for peptide and oligonucleotide synthesisers.

There is thus a need for a flexible set-up where the organic chemist can acquire a number of reagents together with a number of possible sets of reaction parameters, e.g. for optimisation processes. This appears to be especially relevant in the cases where the organic chemist is utilising microwave assisted chemical reactions.

US 5,800,784 describes a chemical treatment cassette for enabling the performance of various complex chemistries with minimal human intervention. It is described that the cassette includes a machine readable code set for identifying the exact chemical treatment protocols required for the samples in the cassette. Thus, the machine readable code set substitutes the manual instructions normally provided to an apparatus so that the cassettes can be processed independent of human intervention. However, in US 5,800,784, the machine readable code set and thereby the exact chemical treatment protocols should still be selected by the user prior to the processing of the samples.

There is, thus, a need for a method for selecting reaction parameters for and conducting a chemical reaction where the user simply by providing information about the chemical structure (or at least the functionality involved in the chemical reaction) of, e.g., a substrate (chemical species) is able have the substrate reacted in the presence of, e.g., a reagent (chemical substance) under suitable conditions or to perform an optimisation process so as to identify substantially optimal reaction condition.

DESCRIPTION OF THE INVENTION

Method for selecting reaction parameters

As mentioned above, the present invention i.a. relates to a method for selecting parameters for a chemical reaction and to a method for conducting a chemical reaction. Generally, the term "chemical reaction" should be interpreted in the broadest sense. Examples of "chemical reactions" range from (a) the formation of new chemical entities (covalent bond formation) via the reaction of a chemical species with one or more reagents optionally under the influence of a catalyst, over (b) formation of salts, (c) racemisation of chemical species, and (d) isomerisation/rearrangement of chemical species, to (e) formation of affinity pairs, e.g. facilitated "receptor"-ligand interaction. For all these types of chemical reactions, an (unknown) optimal set of reaction parameters is believed to exist. It is believed that the present invention will make it possible for a person to gain access to an suitable or even (nearly) optimal set of

reaction parameters and to perform a desired reaction with a minimum of manual optimisation.

The chemical reaction typically involve a chemical species (B; e.g. "a starting material"), a chemical substance (A; e.g. a reagent) and optionally a catalyst (e.g. an enzyme) thereby leading to the desired product (D). Said chemical species (e.g. starting material) can be any chemical entity in any phase, e.g. solid phase, liquid phase or gas phase.

Especially interesting chemical reactions within the present context are organic reactions e.g. polymerisation/oligomerisation, esterification, decarboxylation, hydrogenation, dehydrogenation, addition such as 1,3-dipolar addition, oxidation, isomerisation, acylation, alkylation, amidation, arylation, Diels-Alder reactions such as maleinisation and fumarisation, epoxidation, formylation, hydrocarboxylation, hydroboration, halogenation, hydroxylation, hydrometallation, reduction, sulphonation, aminomethylation, ozonolysis, etc. It is believed that the apparatus and methods according to the invention are especially suited for reactions involving one or more catalysts and for asymmetric organic reactions. It should be understood that the term also includes reactions where enzymes are involved as catalysts, e.g. the polymerase chain reaction (PCR) and similar types of reactions.

The chemical reaction can take place in a suitable solvent or in neat form. Suitable solvents will, as will be acknowledged by the person skilled in the art, depend on the reactions to be conducted. When a solvent is used in a microwave assisted chemical reaction, it is preferred that the dissipation factor (or loss tangent) of the solvent is greater than about 0.04 at 20°C. Examples of suitable solvents for microwave assisted chemical reactions are acetonitrile, DMF, DMSO, NMP, water, tert-butanol, EtOH, benzonitrile, ethylene glycol, acetone, THF and, as a very interesting possibility, ionic liquids.

As mentioned above, one aspect of the present invention relates to a method for selecting sets of reaction parameters for a chemical reaction which is to be conducted in an apparatus which provides energy for the chemical reaction.

With respect to the present description with claims, a chemical reaction can generally be considered as a involving a chemical species ^{X}B (which may be a selected starting material or substrate for the chemical reaction) and resulting in a reaction product ^{X}D (which is the desired product or outcome of the chemical reaction). It should furthermore be understood that the reaction product includes a functionality δ and that the chemical reaction involves a functionality β in ^{X}B, which is transformed into δ in ^{X}D. The prefix "X" indicates that the symbols B and D are associated and they represent the chemical reaction for which the reaction parameters are to be found (yet unknown = X).

Thus, the chemical reaction can generally be considered as the following transformation:

$$^{X}B(\beta) \dashrightarrow {}^{X}D(\delta)$$

where the part of ^{X}B not being included in the functionality β is substantially preserved as the part of ^{X}D not being included in the functionality δ. This being said, especially with due respect to the description further below, the chemical reaction is typically conducted under the influence of a chemical substance A. Such a chemical substance A includes a functionality α which is involved in the transformation of β into δ.

Thus, in a more specific manner, the chemical reaction should be considered as the following transformation:

$$A(\alpha) + {}^{X}B(\beta) \dashrightarrow {}^{X}D(\delta)$$

As an illustrative example, the reaction involve a chemical species ^{X}B (e.g. a starting material selected by the operator of the apparatus wherein the chemical reaction is to be conducted) and resulting in a reaction product ^{X}D (e.g. the desired product) which includes a functionality δ, where the chemical reaction involves a functionality β (e.g. a carboxylic acid functionality) in ^{X}B which is transformed into δ (e.g. an carboxylic ester functionality) in ^{X}D.

In a more specific illustrative example, the chemical species (^{X}B) may be cyclohexyl-1-carboxylic acid and the desired product (^{X}D) may be benzyl cyclohexyl-1-carboxylate, where the functionality β included in ^{X}B is -COOH which is to transformed to the ester -COOBn, thus, δ in ^{X}D is -COOBn. In this instance, A could be BnCl, i.e. α = -Cl.

With reference to the above, the method comprises the following step of providing information to a parameter selection unit about (at least) the functionality β in the chemical species ^{X}B. Thus, as a minimal requirement, information about the functionality β in the chemical species ^{X}B should be provided to a parameter selection unit. Such information might be in the form of structural information about the functionality or information in the form of a code specifically referring to the functionality β. When a user interface module is available in connection with the parameter selection unit, it might be possible to either draw the chemical functionality β and even the partial (more than just the chemical functionality β) or substantially full chemical structure of the chemical species ^{X}B. A user interface module providing this possibility can be made available by using standard software products, e.g. ISIS Draw, etc., used for graphical presentation of chemical structure, as such software products are able to present chemical structures in a standardised manner. Alternatively, the operator might select the functionality from a list of chemical functionalities provided via the user interface module.

It is preferred that at least a partial chemical structure of ^{X}B is provided so as to make is possible for the parameter selection unit to retrieve the most relevant sets of reaction parameters from the database (see below). In particular, the full chemical structure of ^{X}B is provided so as to ensure that other functionalities in ^{X}B are also taken into consideration.

The present method also comprises the step of providing information to the parameter selection unit about the desired transformation of β to δ. This information can, as above for β, be given in the form of structural information about the functionality δ or information in the form of a code specifically referring to the functionality δ or the specific transformation β -> δ. Information about the partial or complete structure need not necessarily to be given as the part of ^{X}D not being δ normally is typically

essentially identical to the part of ^{X}B not being β. Thus, if the full (or partial) structure of ^{X}B is already provided, information about the transformation, or simply about δ, is normally sufficient.

The parameter selection unit is used for retrieving the Q sets of reaction parameters from a database and for selecting R sets of reaction parameters based thereon. Thus, the parameter selection unit preferably includes processing means for conducting the retrieval, processing and selection. As an optional module associated with the parameter selection unit, a storage means (diskette, CD-ROM, semiconductor memory chip, etc.) for either permanent or temporary storage of data can be included. Furthermore, as mentioned above, the parameter selection unit preferably includes a user interface for providing the information about (at least) the functionality β and about the desired transformation of β to δ. Also, the parameter selection unit can include a neural network sub-module for providing the option of maintaining the database with results of the reactions performed (preferably including yields), thereby giving the possibility of reducing the optimisation process.

The present invention also includes the step of providing a database comprising N sets of associated data, each of the N sets comprising (at least):

i) a set of reaction parameters for a (pre-run) chemical reaction involving the transformation of a functionality $^{N}\beta$ of a chemical species ^{N}B into $^{N}\delta$ in a product ^{N}D under the influence of a chemical substance ^{N}A, such chemical substance including a chemical functionality $^{N}\alpha$ being involved in the transformation of the functionality $^{N}\beta$ to the functionality $^{N}\delta$; and

ii) functional or structural information about the chemical species ^{N}B.

The database might have one of many possible formats known to the person skilled in the art. In particular, several commercially available formats are possible, e.g. Beilstein Crossfire, Scifinder, ISIS/Base (Teilheimer, Spore, CIRX, Daylight). The database is provided on a storage means, e.g. a diskette, a hard disk, a CD-ROM, a semiconductor memory chip, etc. In a very interesting embodiment, the database is provided on a storage means which is accessible via the internet. This possibility makes is possible

for the user/customer (via the parameter selection unit) to have access (e.g. via an access code) to a database which is provided and maintained by a supplier.

As mentioned above, the database comprises N sets of "associated data". By the term "associated data" is meant that a series of data representing information about a chemical reaction is presented in the database in a way that will make it possible for the parameter selection unit to retrieve such data. One way of traditionally "organising" the database is to present the associated data in separate records, however, as the database also should comprise functional or structural information about the chemical species ^{N}B, it is envisaged that a relational database often is more suitable.

The positive integer N is also used as a prefix for B, D, β, δ and A thereby indicating that specific B, D, β, δ and A's, respectively, are included in the n'th set (n being in the range of 1 to N) of associated data in the database. It will be apparent that N can be any positive integer, however preferably an integer of at least 4, such as at least 10, in particular at least 25. The total number of sets of associated data may be quite large, e.g. up to 1,000 or even up to 10,000. It should be understood that ^{N}B and ^{N}D in one sets of associated data can be the same as in another set of associated data. Actually, this situation simply implies that the same chemical reaction (the transformation ^{N}B --> ^{N}D) has been performed under different conditions (e.g. involving different A's or different conditions). In particular, the N sets should also comprise sets of associated data corresponding to non-identical sets of ^{N}B and ^{N}B, i.e. not all sets of associated data should relate to the same reaction B --> D.

The N sets of associated data each comprise a set of reaction parameters for a chemical reaction involving the transformation of a functionality $^{N}\beta$ of a chemical species ^{N}B into $^{N}\delta$ in a product ^{N}D under the influence of a chemical substance ^{N}A, such chemical substance including a chemical functionality $^{N}\alpha$ being involved in the transformation of the functionality $^{N}\beta$ to the functionality $^{N}\delta$. Thus, the chemical reactions for which data (sets of reaction parameters) are stored in the database can all be generalised as the transformation

$$^{N}A(^{N}\alpha) + {}^{N}B(^{N}\beta) \rightarrow {}^{N}D(^{N}\delta).$$

In the present context, the term "set of reaction parameters" is intended to mean a specific set of parameters which make is possible to conduct a chemical reaction in a reproducible manner. Typical examples of reaction parameters for chemical reactions are parameters with respect to temperature (i.e. temperature level, temperature cycles, etc.), pressure (i.e. initial pressure, maximum pressure, etc.), reaction time, reaction cycles, relative amounts of reactants, time of addition of reactants, etc. As will be apparent, the associated data may also include information about addition of necessary additional reagents and/or catalysts, etc. Although not mandatory, it will often be advantageous to include information about the yield or the pre-run reactions and optionally also the purity.

The set of reaction parameter may be presented either as the direct parameters (temperature, pressure, etc.) or may be presented as indirect parameters, i.e. control parameters for the apparatus which is to provide energy for the chemical reaction. In the latter instance, the set of reaction parameters is typically presented as a control parameter protocol which will lead to the desired parameters with respect to temperature, pressure, etc. when used in the apparatus. In this instance, it is preferred that the set of reaction parameters also comprises information about the intended parameters with respect to temperature, pressure, etc. in that such additional information can be used to monitor the conducted reaction and, in a even more preferred embodiment, to slightly adjust the control parameters so as to obtain the desired reaction parameters.

Furthermore, it should also be understood that a set of reaction parameters may allow the person in control of the apparatus or an computer associated with the apparatus (e.g. a computer comprising a trained neural network for optimising the reaction conditions) to alter the set of reaction parameters if desirable. However, preferably the parameter selection unit should work without user intervention except where information is required as described for the invention.

The N sets of associated data also each comprise functional and/or structural information about the chemical species ^{N}B. As the minimal information in this regard, information about the functionality $^{N}\beta$ should be given (functional information). As

mentioned above, further information about the partial or full chemical structure (structural information) is preferably also given in order to make it possible to compare the chemical structure of the ^{N}B's and ^{X}B. This will, as mentioned above, make it possible to take into consideration the impact of other potentially reactive functionalities within ^{X}B.

The N sets of associated data preferably also comprises information about the functionality δ, and more preferably also information about the chemical substances ^{N}A, in particular the functionality $^{N}\alpha$, but more preferred also further partial or full structural information.

In an especially interesting embodiment, none of the N sets of associated data in the database exactly correspond to a transformation of ^{X}B into ^{X}D. This means that the desired reaction (involving the transformation of a specific ^{X}B to a specific ^{X}D) has not been performed in advance, and the full impact of the present invention with respect to retrieval and selection can then be exploited.

The method also comprises the further step of allowing the parameter selection unit to retrieve Q sets of associated data (Σ_Q) from the database, such sets of associated data being selected so that the functionality $^{N}\beta$ in each set of associated data is essentially identical to the functionality β in ^{X}B and the functionality $^{N}\delta$ is essentially identical to δ in the product ^{X}D. The term "essentially identical" indicates that the functionalities taken as such should be structurally identical, but that certain differences might appear, especially with respect to reactivity (electron distribution, sterical hindrance, etc.).

It will be apparent that the provided information about $^{X}\beta$ and $^{X}\delta$ should have the same level of specificity as the information about $^{N}\beta$ and $^{N}\delta$. This should be taken into consideration when constructing the parameter selection unit and building the database.

It is envisaged that the result of the desired reaction (or reactions in an optimisation procedure) can be provided to the database so as to extend the knowledge

accumulated. In connection herewith, it is relevant to provide information about the yield and optionally also about the purity.

Yield (and purity), when incorporated in the sets of associated data will give the intriguing possibility for the operator to define a certain threshold value for the yield when processing the Q sets of data. It is also envisaged that the operator can define a maximum for the number of reactions to be performed, i.e. a maximum for R.

It should also be understood that the apparatus typically (and preferably) retrieves more than one set of reaction parameters ($Q > 1$), if such are available in view of the requirements above.

It will be apparent that Q can be any positive integer ($Q <= N$). Preferably Q is more than 1. The positive integer Q is also used as a prefix thereby referring to the q'th set (q being in the range of 1 to Q) of retrieved data.

The method also comprises the further step of processing the Q sets of associated data (Σ_Q) in order to obtain the R sets of reaction parameters ($^X\Sigma_R$).

In the general aspect, R sets of reaction parameters are selected, where R is an integer of at least 1. As will be apparent from the following, the embodiment where R is above 1 represent the general optimisation aspect where R ($R > 1$) sets of reaction parameters are selected, thereby making it possible to conduct R chemical reactions under fairly realistically reaction conditions. As will be apparent, such an optimisation procedure may be conducted in an iterative manner. The embodiment where only one set of reaction parameters is selected represents the aspect where the best guess for a suitable set of reaction parameters is identified.

In the present method, it is typically preferred that the reaction of ^XB to give the product ^XD under the conditions defined by the sets of reaction parameters ($^X\Sigma_R$) require the influence of corresponding chemical substances A_R, where such chemical substances A_R including a chemical functionality α_R being involved in the transformation of the functionality β to the functionality δ. In this preferred variant, it

is thus important that the R sets of reaction parameters also comprise information about which specific A_R's are required.

The chemical substances A_R should preferably be selected so that the functionalities α_R thereof resemble the functionalities ${}^N\alpha$ of the chemical substances ${}^NA$ retrieved as in the Q sets of associated data (Σ_Q). Thus, the reagents proposed with the R sets of reaction parameters should preferably be of the same type as the ones used in the pre-run reactions represented in the database. ($\alpha_R \cong {}^N\alpha$)

Thus, preferable, the R sets of reaction parameters (${}^X\Sigma_R$) are accompanied by corresponding information about the chemical substances A_R under which influence the R reactions should be conducted. Such information should, beside the information about the functionality or (full or partial) structure of the A_R's, also comprise information about the amount of chemical substance (number of equivalents), time of addition, etc.

This, being said, it is also preferred that the Q sets of associated data which are to be retrieved from the database also include information about any additional constituents involved in the chemical reaction involving the transformation of a functionality ${}^N\beta$ of a chemical species ${}^NB$ into a ${}^N\delta$ in a product ND under the influence of a chemical substance ${}^NA$. Such additional constituents may include catalysts, additional reagents, solvents, reactive gasses, inert atmospheres, etc. In connection therewith, it is of course particularly relevant that the R sets of reaction parameters (${}^X\Sigma_R$) are accompanied by information about any such additional constituents involved in the chemical reaction.

As such additional constituents are not necessarily all readily available for the operator of the apparatus, the R sets of reaction parameters (${}^X\Sigma_R$) are preferably selected based on the processing of the Q sets of associated data (Σ_Q) taking into consideration the availability of chemical substances (A_R) and any additional constituents involved in the chemical reaction. Information about availability can either be provided the to parameter selection unit by the user or provided via the apparatus. In an especially interesting embodiment, the apparatus is constructed in a manner so that it is possible

to keep track of availability of various reagents, catalysts, etc. In an other embodiment, the operator of the apparatus is prompted by the apparatus or parameter selection unit to indicate whether certain additional constituents are available. In this connection it is envisaged that the database can be linked to a Chemical inventory management system (i.e. CIMS, an MDL product) or a Available chemical directory (ACD in ISIS/Base).

In the methods according to the present invention, chemical substances A_R are preferably reagents. In an especially intriguing variant, the chemical substances A_R are immobilised. This can be especially interesting when the chemical reaction is a formation of an affinity pair (e.g. capture) or when a solid phase synthesis is performed.

In an interesting embodiment, ${}^{X}\Sigma_R$ comprises only one set of reaction parameters, i.e. $R = 1$. Within this embodiment, it is envisaged that the retrieved Q sets of reaction parameters are processed so as to provide a set of reaction parameters based on the best substructural match between ${}^{X}B$ and the ${}^{N}B$'s in Σ_Q, i.e. one set of reaction parameters corresponding to a pre-run reaction which included a similar chemical species. Alternatively, the retrieved Q sets of reaction parameters are processed so as to provide a set of reaction parameters based on weighed average of the sets of reaction parameters in Σ_Q. In particular, the weighing of the sets of reaction parameters in Σ_Q is performed based on the structural similarity between ${}^{X}B$ and the ${}^{N}B$'s in Σ_Q.

The terms "structural match" and "structural similarity" refer to comparative measure which can be performed by available software products incorporated in or collaborating with the parameter selection unit. It should be understood that structural similarity or structural match can also be based on a preselected substructure of the molecule. This is apparent as the information provided to the parameter selection unit may be limited to a substructure of ${}^{X}B$. In order for the parameter selection unit to perform the comparison, one of a number of possible commercial software products can be associated with the parameter selection unit. Examples hereof are ISIS/Base and Beilstein Crossfire and Scifinder as well as several molecular modelling software packages.

In another interesting embodiment, $R = Q$ and ${}^{x}\Sigma_R$ is a substantially identical to Σ_Q, i.e. the parameters from the retrieved Q sets are simply used directly as parameters in the R sets of reaction parameters, preferably by using A_R's having the same functionalities α_R as the functionalities ${}^{N}\alpha$ in the corresponding reaction.

In still another embodiment, $R > 1$, i.e. the R sets of reaction parameters can be used in an optimisation process. Preferably, the R sets of reaction parameters involves the use of more than one chemical substance A_R. In this manner, various types of chemical substances (e.g. reagents) can be tested under various conditions in an optimisation process (R reactions). In particular, when an initial optimisation process is conducted in order to identify a chemical substance A to be used in a subsequent optimisation process, the R sets of reaction parameters involves the use of R chemical substances A_R. It will be appreciated that various interesting variants exist within this embodiment. It should be understood, that in the cases where various A's are to be tested, the R sets of reaction parameters should include such information. In one variant, the R sets involve a few A's in combination with a number of different solvent, catalysts, temperature profiles, etc. thereby yielding a complete set for optimisation suggestions.

Alternatively, in an optimisation process, information about preselected ${}^{x}A$'s are provided to the parameter selection unit, thereby allowing the parameter selection unit to take into consideration the availability of chemical substances (reagents) in the processing of the Q sets (selection step). This, embodiment, which may be combined with the above embodiment, is especially relevant where the operator needs specific information about applicability of a preselected reagent or reagent range.

In an optimisation process where the present method is used for selecting reaction parameters, it is advantageous to include information about the yields of the respective reactions in the Q retrieved sets and in the R selected sets so as to facilitate subsequent iterations in a multi-step optimisation process.

A kit and a method involving the use of a kit

In view of the above, the present invention also provides a kit for optimising the reaction conditions for a preselected chemical reaction (transformation) which is to be conducted in an apparatus which provides energy for the chemical reaction,

said kit comprising

(a) P containers each comprising a chemical substance A_R including a chemical functionality α_R which (at least theoretically) can facilitate the transformation of a functionality β to a functionality δ in a chemical reaction involving a chemical species ^xB, said chemical reaction being intended to result in a reaction product ^xD which includes a functionality δ, where the chemical reaction involves a functionality β in ^xB which is transformed into δ in ^xD,

(b) a data carrier comprising R sets of reaction parameters $^x\Sigma_R$, each set of reaction parameters corresponding the transformation of β into δ under the influence of the functionality α_R of a chemical substance A_R.

The present invention also relates to a method for optimising the reaction conditions for a preselected chemical reaction which is to be conducted in an apparatus which provides energy for the chemical reaction, said chemical reaction involving a chemical species ^xB and being intended to result in a reaction product ^xD which includes a functionality δ, where the chemical reaction involves a functionality β in ^xB which is transformed into δ in ^xD, said method comprising the use of a kit as defined herein.

It should be understood that the parameters, symbols, etc. have the meaning defined above. The positive integer P indicates the number of different chemical substances to be used in the R reactions. P is typically >1, such as >3. It should be understood that one chemical substance may be used in several reactions within the method for optimising reaction conditions (thus, $P <= R$).

The data carrier in the kit may be any storage means for carrying data, e.g. diskette, CD-ROM, semiconductor memory chip, etc. In an alternative variant, the data carrier may be accessible from the internet, and the kit could then include an access code for

the internet data carrier. The access code may be provide on a SmartCard or simply on paper. It is especially preferred that the data carrier is a semiconductor memory chip (e.g. a SmartCard), which easily can be provided with the R sets of information .

It is preferred that the reaction parameters for the R possible chemical reactions have been selected by using the method for selecting reaction parameters defined herein, of course taking into consideration the P chemical substances which are included in the kit.

The kit and the method for optimisation is preferably performed in a microwave apparatus.

Method of conducting a chemical reaction

The present invention also relates to a method of conducting R chemical reactions in an apparatus which provides energy for the chemical reactions, said chemical reaction involving a chemical species ^{X}B and resulting in a reaction product ^{X}D which includes a functionality δ, where the chemical reaction involves a functionality β in ^{X}B which is transformed into δ in ^{X}D, each reaction being performed under the influence of a corresponding chemical substance A_R, such chemical substances A_R including a chemical functionality α_R being involved in the transformation of the functionality β to the functionality δ,

the method comprising

* selecting a plurality of sets of reaction parameters in accordance with the method defined above;

* providing an array of R reaction mixtures each comprising a predetermined amount of the chemical substance A_R and the chemical species ^{X}B and any additional constituents required according to the sets of reaction parameters;

* treating each of the R reaction mixtures in the apparatus in accordance with the corresponding set of reaction parameters.

The R reactions typically use P different reagents (A_R) as above.

In a particularly interesting embodiment, which can be realised when using the microwave apparatus described herein, treatment of the R reactions is performed substantially simultaneously. Alternatively, the reactions are performed sequentially.

As described above, the treatment typically includes heating. Preferably, the reaction is a microwave facilitated chemical reaction, wherein treatment is application of microwaves. Such a reaction is preferably performed in a microwave apparatus.

Such a microwave apparatus preferably comprises a controllable microwave generating and amplification means, i.e. the apparatus is preferably of the type described herein. When such an apparatus is used, the application of microwaves is preferably controlled by the R selected set of reaction parameters via the controllable microwave generating and amplification means.

Preferred microwave apparatus

The chemical reaction is performed in "an apparatus which provides energy for the chemical reaction". In general, it should be mentioned that "providing energy of the chemical reaction" is intended to mean that the apparatus in question provides activation energy for the chemical reaction. As a typical side effect of this heating occur. It is envisaged, especially when the apparatus is a microwave apparatus, that activation by using a very specific frequency of electromagnetic radiation will provide sufficient activation energy for a chemical reaction to occur (activation of the reactants) without any significant heating. The term is however intended to cover a number of conventional apparatuses for heating as well as more advanced apparatuses, e.g. microwave apparatuses, preferably such microwave apparatuses having controllable microwave generating and amplification means. It should be understood that the apparatus might comprise further facilities, e.g. facilities for cooling (e.g. for a PCR set-up), pressurising, application of an inert atmosphere, etc.

In connection with a microwave apparatus, it is preferred that the Q sets of reaction parameters are provided in the form of control parameters for the apparatus.

The term of "in an apparatus" is not intended be limiting.

In a preferred embodiment, the apparatus is a microwave apparatus. In particular, the reaction is a microwave facilitated chemical reaction, wherein heating is obtained with microwaves. This can be obtained in a very advantageous manner in the case where said microwave apparatus comprises a controllable microwave generating and amplification means. This will make it feasible, in a still more preferred embodiment, to allow the heating with microwaves to be controlled by the selected set of reaction parameters via the controllable microwave generating and amplification means.

In the present context, the term "microwave" refer to electromagnetic radiation having a frequency in the range of 300 MHz-300 GHz.

A preferred apparatus to be used in connection with the methods according to the present invention is a microwave apparatus, in particular a microwave apparatus comprising a controllable microwave generating and amplification means.

One possible - and presently preferred - apparatus is an apparatus for providing an electric signal at a plurality of frequencies, the apparatus comprising:

a) generating means for generating a first electric signal, said generating means having an input and an output terminal,

b) amplifying means for amplifying the generated first electric signal, said amplifying means having an input and an output terminal, wherein the input terminal is operationally connected to the output terminal of the generating means,

c) power means for providing power to the input terminals of the generating means and the amplifying means, and

d) control means for providing a first control signal to the generating means and for providing a second control signal to the amplifying means,

wherein, that the generating means and the amplifying means are essentially constituted by semiconductor components.

Among the advantages of such an apparatus to be used in connection with the present invention can be mentioned:

- The possibility of conducting parallel (simultaneous) chemical reactions in the optimisation process in that individually settings of reaction parameters (such as frequency, power, temperature, pressure etc.) can be set for each individual sample
- The possibility of parallel monitoring of a plurality of chemical reactions with individually monitoring of process parameters such as frequency, power, temperature, pressure etc.
- The possibility of parallel (simultaneous) control of a plurality of chemical reactions with individually adjustments of process parameters such as frequency, power, temperature, pressure etc.
- The possibility of varying the frequency of the applied energy

Figure 1 illustrates a preferred elaborate variant of the microwave apparatus. In the especially interesting variant of the apparatus comprises a semiconductor based signal generator 28, a drive amplifier 29 for amplifying the generated signal, a power amplifying 30 for further amplification, a circulator 31 for preventing a back-reflected signal from entering the power amplifier, a bi-directional coupler 32 for retrieving signal travelling in both directions, a distributing network for transmitting power to the microwave cavity 24. The cavity comprises a plurality of sample inlets and outlets 38-41, a transmitting device 42 and a receiving device 13. Further, the cavity comprises an atmosphere in/out port 15.

In order to determine the power transmitted to and reflected from the cavity the apparatus, in the preferred embodiment, further comprises four power meters 34-37. Power meter 34 measures the reflected power from the cavity, power meter 35 measures a portion of the power delivered to the cavity, power meter 36 measures a

portion of the power reflected by the cavity, whereas the power measured by power meter 37 is a measured of the absorbed power in the sample.

The overall apparatus is controlled by a controller 45 which is adapted to receive power information from the four power meters and to provide control signals to the generator and to the drive and power amplifier. The controller is operationally connected to a PC 43 and a common power supply 44.

Figure 2 describes a simple variant of the apparatus according to the invention. As seen in the figure the apparatus comprises a semiconductor based microwave generator and semiconductor based amplifier. The apparatus further comprises a control unit and a power supply unit. The control unit is adapted to provide a first control signal to the generator so as to control the frequency of the generator. Further, the control unit provides a second control signal to the amplifier so as to control the amplification of the generated signal. The second control signal may also determine the time dependency of the amplified signal, i.e. how the amplified signal shall depend on time.

Figure 2 further illustrates a distribution network being capable of transmitting the amplified signal to a single microwave cavity or to a plurality of cavities so as to operate a plurality of cavities in parallel.

The generating means and the amplifying means are essentially constituted by semiconductor components. The semiconductor based signal generator is the device by which an electric signal is generated. The generated signal could continuously vary between 300 MHz-300 GHz. The power of the output signal could continually vary between 0 and 1 W. The output of the signal generator is capable of driving a driver or power amplifier. The signal generator is controllable/programmable from a controlling device. The control functions are in the form of controlling the amplitude, frequency, signal form, pulse form, duration of the signal/pulse and any combinations of two or more functions at the same time.

The amplifying means may comprise a driver amplifier and a power amplifier. The driver amplifier is a semiconductor based device being adapted to amplify the

magnitude of the signal from the signal generator. The gain of the driver amplifier is adjustable by varying the level of a control signal. Thus the magnitude of the output may be selected by the operator.

The power amplifier is provided for processing the signal from the driver-amplifier. The power amplifier is a semiconductor based device with a adjustable gain. The gain may be varied by varying the level of a control signal. The output power of the power amplifier is typically in the kW range.

The amplified signal from the amplifying means is distributed to one or more microwave cavities using a distributing network, wherein the one or more microwave cavities may be single mode cavities.

The apparatus further comprising a circulator being adapted to be operationally connected between the amplifying means and the distributing network, said circulator having at least one input terminal, an output terminal and at least one combined input/output terminal, wherein the input terminal is operationally connected to the output terminal of the amplifying means and wherein the combined input/output terminal is operationally connected to the distribution network. Furthermore a load and a power determining means may be incorporated in the apparatus, wherein the load is operationally connected to the output terminal of the circulator and wherein the power determining means is operationally connected to the load and the control means.

The circulator prevents the reflected power from the microwave cavity from entering the power amplifier. Instead the reflected power is directed to an dummy load which is operationally connected to a power meter.

The apparatus further comprises a coupler, such as a bi-directional coupler, being adapted to be operationally connected between the circulator the distribution network, said coupler having an input terminal, at least two output terminals and one combined input/output terminal, said input terminal being operationally connected to the output terminal of the circulator and wherein the output terminal is operationally connected to the distributing network.

The apparatus further comprising two power measuring means, said power measuring means being operationally connected to the output terminals of the coupling means and said power determining means being operationally connected to the control means.

The bi-directional coupler directs a fraction of the input and/or the reflected power to two power meters. One of the power meters measures a portion of the power travelling in the direction towards the microwave cavity, whereas the second power meter measures a portion of the power travelling in the opposite direction, i.e. away from the microwave cavity.

In a preferred embodiment, the apparatus comprises a total of four power meters. A first power meter measures the reflected power from the microwave cavity. A second power meter measures the input power provided to the microwave cavity. A third power meter measures the reflected power from the microwave cavity at a different position than the first power meter. Finally a fourth power meter measures the power coupled to the sample.

The microwave cavity comprises an output terminal, said output terminal being adapted to be operationally connected to a load that anticipates the reflected power from the microwave cavity. Furthermore, a power measuring means is operationally connected to the load and the control means

The controller has a central function as showed in figure 1. The controlling device is a (micro)computer based system for controlling (run-time control) and programming of the apparatus and all its modules/components.

The controller might be connected to one or several PCs´ in a network as a user interface and/or computing device for one or several microwave apparatuses. In this way storage means for storing data and/or processed data and/or data concerning predetermined process parameters are available. This part of the apparatus is typically operationally connected with the parameter selection unit.

The output frequency of the generator means is adjustable so as to vary the frequency of the generated electromagnetic field. The output frequency of the semiconductor generator is in the range from 300 MHz-300 GHz, e.g. from 500 MHz-300 GHz such as 500 MHz-10 GHz or 2-30 GHz.

When the microwave apparatus is used in connection with the methods of the present invention, the reaction chamber is microwave cavity which comprises

a) a resonance chamber having an input terminal,

b) means for irradiating a microwave signal inside the resonance chamber, said irradiating means being operationally connected to the input terminal of the resonance chamber.

The irradiating means may be movable so as to vary the level of signal coupled to the rod from the irradiating means. Means for adjusting the length of the rod comprises a first and a second cylinder, wherein the first cylinder is positioned inside the second cylinder and wherein the rod is positioned inside the first cylinder. The first and second cylinders are movable relative to each other and wherein the first cylinder is movable relative to the rod so as to adjust the length and thereby adjust the resonance frequency of the cavity.

The first control signal provided to the generating means by the control means varies according to a first function of a signal back-reflected from the microwave cavity, said back-reflected signal being detected by one of the power measuring means operationally connected to the coupling means. The second control signal provided to the amplifying means by the control means varies according to a second function of a signal back-reflected from the microwave cavity, said back-reflected signal being detected by one of the power measuring means operationally connected to the coupling means.

The first control signal provided to the generating means determines the output frequency of the generating means. The second control signal provided to the

amplification means determines the amplitude of the amplified signal. The amplitude of the amplified signal may varied as a function of time.

The control system has three different modes of operation: 1) heating mode, 2) monitoring mode, and 3) programming mode.

The apparatus is adapted for heating two or more reaction mixtures simultaneously and/or sequentially and/or intermittently. The microwave cavities may be single mode cavities.

Operating the controller in heating mode puts specific requirements to the configuration of the controller. The controller is capable of setting and controlling the output power from the drive amplifier and the power amplifier. Furthermore, the controller is capable of modulating the signal generated by the signal generator so as to generate an output signal which is a function of time such as a rectangular or triangular wave form. In the same context, the duty circle of the signal must be adjustable so as to reduce the power of the delivered signal.

The above-mentioned control facilities is provided by applying a first control signal to the drive amplifier and a second control signal to the power amplifier.

Another feature which can be the incorporated in the controller is the ability to control the output frequency of the signal generator. Also the settings relating to frequency scans, i.e. start frequency, stop frequency, frequency resolution and scan time must be controllable from the controller.

The starting frequency is in the range of 0.5-300 GHz, preferably in the range of 1-30 GHz. Predetermined values between which the frequency of the electromagnetic field is varied are in the range of 0.5-300 GHz, preferably in the range of 1-30 GHz.

Furthermore, the process time for a complete process or parts of a process if it involves more than one step should be controllable.

Measuring the input power to the microwave cavity by means of a power meter 35 (figure 1) is accomplished. Furthermore, the reflected power from the microwave cavity is also measured with power meters 34 or 37. Finally, the power absorbed power in the microwave cavity is measured. This may be done by firstly calibrate the apparatus with an empty cavity to measure the losses in the cavity. The calibration may be done within the frequency range where the sample is to be processed. By subtracting the reflected power and the loss power of an empty cavity the absorbed power can be calculated.

The power signal measured by the power meters are transmitted to the controller so as to be used for controlling the frequency of the signal generator and/or the gain in the driver-amplifier and/or the power amplifier.

The controller may also provide control signals for system components - such as directional couplers, circulators etc. Varies types of signal processing may also be provided by the controller.

It is possible to set a maximum value not to be exceeded during the process and a minimum value not to fall below during the process. Concerning pressure, it is possible to set a maximum value not to be exceeded during the process and a minimum value not to fall below during the process.

In the monitoring mode a scan function that normalises the signal from a first scan (gives a strait baseline) and detects the difference from the normalised baseline during a number of subsequent scanning cycles is available.

Tracking and locking to the frequency that gives maximum transmitted power into the sample, (moving maxima) is another available feature. The frequency of the microwave generator is adjustable to an extent of at least ± 30% around a centre frequency

Determining the coupling between the electromagnetic field and the sample and varying the frequency and power of the field is essential. Furthermore, the frequency of the electromagnetic field may be changed in response to a change of the level of

the feed-back signal by more than a predetermined threshold value and corresponding data of frequency and coupling efficiency between the electromagnetic field and sample are stored in a memory for further processing.

When the apparatus operates in programming mode the possibility of creating, storing, retrieving and editing using an in-built high level method programming language must be available for the operator. This is especially relevant in an iterative optimisation process. A method is a pre-programmed sequence of events where every event has at least one process as input. A process parameter is e.g. power, time pressure etc.

The receiving antenna (13) can be used for monitoring and receiving the microwaves transmitted through the sample (1) and transfers the energy to a power dissipating device (47) and a power meter (37) via an output signal and power cable (11). The difference between the input power and the output power measured with the power meter (47) mounted on to receiving loop antenna (18b) indicates the sum of in the sample absorbed energy and the total system energy losses. The cavity module of the apparatus can be calibrated by measuring the system losses of the unloaded cavity before the sample is introduced into the cavity. Together with the measured reflected energy from the power input port (10) on the cavity, the system loss will characterise the measured sample in terms of dielectric properties at a given temperature and frequency. By scanning the frequency within a given range, e.g. 1-4 GHz, and monitoring the transmitted signal from the receiving antenna (13) it will be possible to follow the progress of a chemical reaction.

The power supply generate the needed power to support the apparatus in terms of energy for heating the sample and power to the other modules in the apparatus.

Referring now to figure 1 an apparatus for microwave assisted chemical and *biological* reactions is illustrated. One of the main features of the apparatus aims at optimising the reaction conditions for said chemical reaction. Another set of features of the apparatus aims at monitoring and controlling the optimised conditions for said chemical reaction. Yet another set of features aiming at process data collection, data processing, storing and retrieving data from an internal and/or an external database.

When two or more starting materials reacts chemically they are subject to changes in their physical and chemical properties. These changes in properties are usually temperature dependent. Chemical reactions are often performed at elevated temperature to enhance the speed of the reaction or supply enough energy to initiate and maintain a reaction. The form of the supplied energy could be thermal radiation, ultrasound, microwaves etc. In the case of microwaves as supplied form of energy the transferred energy into the reacting materials is dependent of the dielectric properties of the starting and formed materials during the chemical reaction. The dielectric properties are temperature dependent and will therefore vary during the chemical process. Changes in dielectric properties will also take place due to forming of new materials in the chemical reaction. Materials dielectric properties are also known to changes with the frequency.

In a tuned apparatus an optimum of coupled energy into the reaction will occur at a specific frequency. This frequency will change according to the temperature in the reaction in accordance with the dependence of the permitivity ε' of the sample.

Said apparatus also comprising a means of collecting and processing all process data and store and/or retrieve said data from an internal and/or external database.

By using an apparatus with said monitoring and controlling means combined with at least one of the following parameters to be variable: frequency, waveform, power, time, temperature, pressure, artificial atmosphere, it is possible to optimise and maintain these optimal conditions for said chemical reaction.

A distribution network is provided for distributing the electric signal generated and amplified using the semiconductor signal generator and the semiconductor amplifiers respectively. The generated and amplified signal may be distributed to a single or to a plurality of microwave cavities. In the case of having a plurality of the microwave cavities the microwave cavities may be operated in parallel.

General guidelines and instructions for the work with microwaves and the constructions of microwave cavities are, e.g., given in Gabriel, et al., Chem. Soc. Rev,

1998, Vol. 27, pp 213-223 and in Microwave Engineering, Harvey (ed.), Academic Press, London 1963 (in particular Chapters 4-6).

The reaction mixture (sample 1) can be placed directly in the cavity, but the sample is typically place in an open or closed sample holder (2). This sample holder (2) cam be an integral part of the cavity or a separate reaction vessel of any material suitable for use in microwave heating applications. As will be know to the person skilled in the art. the material constituting the sample holder should preferably not absorb the microwave energy. Various types of polymers and glasses can be used. Specifically, various types of trays, microtiter plates, etc. can preferably use when a plurality of samples are heated simultaneously. In order to avoid contamination, the sample holder preferably includes a lid.

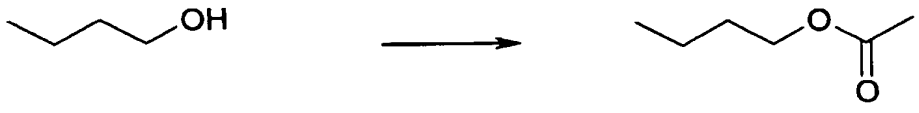
The free space in the cavity can be filled with an inert gas in order to avoid reaction between the gasses and the sample. It is however preferred that the sample holder includes a lid. It is preferred that the cavity includes at least one inlet/outlet for providing an inert atmosphere to the space above the cavity. Alternatively, the space above the sample is filled with a reactive gas, e.g. H_2 which is useful in hydrogenation reactions.

The cavity should preferably be able to sustain high internal pressure either caused by the chemical reaction or intentionally to create a high-pressure atmosphere as a reaction parameter. High internal pressure is normally used as a method to increase the temperature in the reaction vessel over the boiling point for the liquid phase in the reaction vessel. The pressure can be kept at a predetermined level or pre-set as a level not to be exceeded or fall below. The pressure system incorporates a safety valve function for protection of the pressurised components and personal safety of the operator.

EXAMPLES

An illustrative example is given in the following:

The following product is to be synthesised



^{x}B ^{x}D

The first step it to make an exact match search of the functionality β (-OH) and the structure (^{x}B = n-butanol) and the functionality δ (-O-Acetyl).

In the database, it is assumed that several hits (Q') relating to different A, catalyst, solvent, reaction profile etc. are obtained. As an option, it is possible to indicate in a hit list whether the additional constituents called for by the Q' sets are available chemicals. This will often reduce the number of hits. Another possibility is to reduce the number of hits by setting a yield threshold, or a reaction time threshold, etc. This procedure will reduce the number of Q sets of reaction parameters.

The sets of reaction parameters can then be processed to yield the R sets of reaction parameters. If only one hit is left, the Q (Q = 1) reaction parameters may simply be used as $^{x}\Sigma_{R}$.

If not hits are identified by the performed similarity search for the above reaction, a substructural search based on the following substructures

could then be performed: functionality β (-OH) and the substructure (^{x}B = $-CH_2-CH_2-$OH) and the functionality δ (-O-Acetyl).

As above, the next step could be to reduce the number of hits by checking the availability of the chemicals called for. Further reduction of the hit set might be performed, and eventually, the Q sets of reaction parameters is processed into the R sets of reaction parameters.

CLAIMS

1. A method for selecting R sets of reaction parameters (${}^{X}\Sigma_{R}$) for a chemical reaction which is to be conducted in an apparatus which provides energy for the chemical reaction, said chemical reaction involving a chemical species ${}^{X}B$ and resulting in a reaction product ${}^{X}D$ which includes a functionality δ, where the chemical reaction involves a functionality β in ${}^{X}B$ which is transformed into δ in ${}^{X}D$,

the method comprising:

* providing information to a parameter selection unit about the functionality β in the chemical species ${}^{X}B$;

* providing information to the parameter selection unit about the desired transformation of β to δ;

* providing a database comprising N sets of associated data, each of the N sets comprising

i) a set of reaction parameters for a chemical reaction involving the transformation of a functionality ${}^{N}\beta$ of a chemical species ${}^{N}B$ into ${}^{N}\delta$ in a product ${}^{N}D$ under the influence of a chemical substance ${}^{N}A$, such chemical substance including a chemical functionality ${}^{N}\alpha$ being involved in the transformation of the functionality ${}^{N}\beta$ to the functionality ${}^{N}\delta$; and

ii) functional or structural information about the chemical species ${}^{N}B$;

* allowing the parameter selection unit to retrieve Q sets of associated data (Σ_{Q}) from the database, such sets of associated data being selected so that the functionality ${}^{N}\beta$ in each set of associated data is essentially identical to the functionality β in ${}^{X}B$ and the functionality ${}^{MN}\delta$ is essentially identical to δ in the product ${}^{X}D$;

* processing the Q sets of associated data (Σ_{Q}) in order to obtain the R sets of reaction parameters (${}^{X}\Sigma_{R}$).

2. A method according to claim 1, wherein the reaction of ${}^{X}B$ to give the product ${}^{X}D$ under the conditions defined by the sets of reaction parameters (${}^{X}\Sigma_R$) require the influence of corresponding chemical substances A_R, such chemical substances A_R including a chemical functionality α_R being involved in the transformation of the functionality β to the functionality δ.

3. A method according to claim 2, wherein the chemical substances A_R are selected so that the functionalities α_R thereof resemble the functionalities ${}^{N}\alpha$ of the chemical substances ${}^{N}A$ retrieved as in the Q sets of associated data (Σ_Q).

4. A method according to claim 2 or 3, wherein the R sets of reaction parameters (${}^{X}\Sigma_R$) are accompanied by corresponding information about the chemical substances A_R under which influence the R reactions should be conducted.

5. A method according to any of the preceding claims, wherein the Q sets of associated data which are to be retrieved from the database also include information about any additional constituents involved in the chemical reaction involving the transformation of a functionality ${}^{N}\beta$ of a chemical species ${}^{N}B$ into a ${}^{N}\delta$ in a product ${}^{N}D$ under the influence of a chemical substance ${}^{N}A$.

6. A method according to claim 5, wherein the R sets of reaction parameters (${}^{X}\Sigma_R$) are accompanied by information about any additional constituents involved in the chemical reaction.

7. A method according to any of the claims 4-6, wherein the R sets of reaction parameters (${}^{X}\Sigma_R$) are selected based on the Q sets of associated data (Σ_Q) taking into consideration the availability of chemical substances (A_R) and any additional constituents involved in the chemical reaction.

8. A method according to any of the preceding claims, wherein ${}^{X}\Sigma_R$ comprises only one set of reaction parameters (R = 1).

9. A method according to claim 8, wherein the retrieved Q sets of reaction parameters are processed so as to provide a set of reaction parameters based on the best substructural match between ^{X}B and the ^{N}B's in Σ_Q.

10. A method according to claim 8, wherein the retrieved Q sets of reaction parameters are processed so as to provide a set of reaction parameters based on weighed average of the sets of reaction parameters in Σ_Q.

11. A method according to claim 10, wherein weighing of the sets of reaction parameters in Σ_Q is performed based on the structural similarity between ^{X}B and the ^{N}B's in Σ_Q.

12. A method according to any of the claims 1-7, wherein $R = Q$ and $^{X}\Sigma_R$ is a substantially identical to Σ_Q.

13. A method according to any of the claims 1-7, wherein $R > 1$.

14. A method according to claim 13, wherein the R sets of reaction parameters involves the use of more than one chemical substance A_R.

15. A method according to claim 14, wherein the R sets of reaction parameters involves the use of R chemical substances A_R.

16. A method according to any of the preceding claims, wherein the apparatus which provides energy for the chemical reaction is a microwave apparatus.

17. A method according to any of the preceding claims, wherein the Q sets of reaction parameters are provided in the form of control parameters for the apparatus.

18. A method according to any of the preceding claims, wherein none of the N sets of associated data in the database exactly correspond to a reaction of ^{X}B into ^{X}D.

19. A kit for optimising the reaction conditions for a preselected chemical reaction (transformation) which is to be conducted in an apparatus which provides energy for the chemical reaction,

said kit comprising

(a) P containers each comprising a chemical substance A_R including a chemical functionality α_R which (at least theoretically) can facilitate the transformation of a functionality β to a functionality δ in a chemical reaction involving a chemical species ^xB, said chemical reaction being intended to result in a reaction product ^xD which includes a functionality δ, where the chemical reaction involves a functionality β in ^xB which is transformed into δ in ^xD,

(b) a data carrier comprising R sets of reaction parameters $^x\Sigma_R$, each set of reaction parameters corresponding the transformation of β into δ under the influence of the functionality α_R of a chemical substance A_R.

20. A kit according to claim 19, wherein the reaction parameters for the R possible chemical reactions have been selected by using the method defined in any of the claims 1-18.

21. A method for optimising the reaction conditions for a preselected chemical reaction which is to be conducted in an apparatus which provides energy for the chemical reaction, said chemical reaction involving a chemical species ^xB and being intended to result in a reaction product ^xD which includes a functionality δ, where the chemical reaction involves a functionality β in ^xB which is transformed into δ in ^xD, said method comprising the use of a kit as defined herein.

22. A method according to claim 21, wherein the apparatus is a microwave apparatus.

23. A method of conducting R chemical reactions in an apparatus which provides energy for the chemical reactions, said chemical reaction involving a chemical species

^{x}B and resulting in a reaction product ^{x}D which includes a functionality δ, where the chemical reaction involves a functionality β in ^{x}B which is transformed into δ in ^{x}D, each reaction being performed under the influence of a corresponding chemical substance A_R, such chemical substances A_R including a chemical functionality α_R being involved in the transformation of the functionality β to the functionality δ,

the method comprising

* selecting a plurality of sets of reaction parameters in accordance with the method defined in any of the claims 1-18;

* providing an array of R reaction mixtures each comprising a predetermined amount of the chemical substance A_R and the chemical species ^{x}B and any additional constituents required according to the sets of reaction parameters;

* treating each of the R reaction mixtures in the apparatus in accordance with the corresponding set of reaction parameters.

24. A method according to claim 23, wherein treatment of the R reactions is performed substantially simultaneously.

25. A method according to claim 23, wherein treatment of the R reactions is performed sequentially.

26. A method according to claim 23, wherein the treatment includes heating.

27. A method according to any of the claims 23-26, wherein the reaction is a microwave facilitated chemical reaction, wherein treatment is application of microwaves.

28. A method according to claim 27, wherein the apparatus is a microwave apparatus.

29. A method according to claim 28, wherein said microwave apparatus comprises a controllable microwave generating and amplification means.

30. A method according to claim 29, wherein the application of microwaves is controlled by the R selected set of reaction parameters via the controllable microwave generating and amplification means.

Figure 1

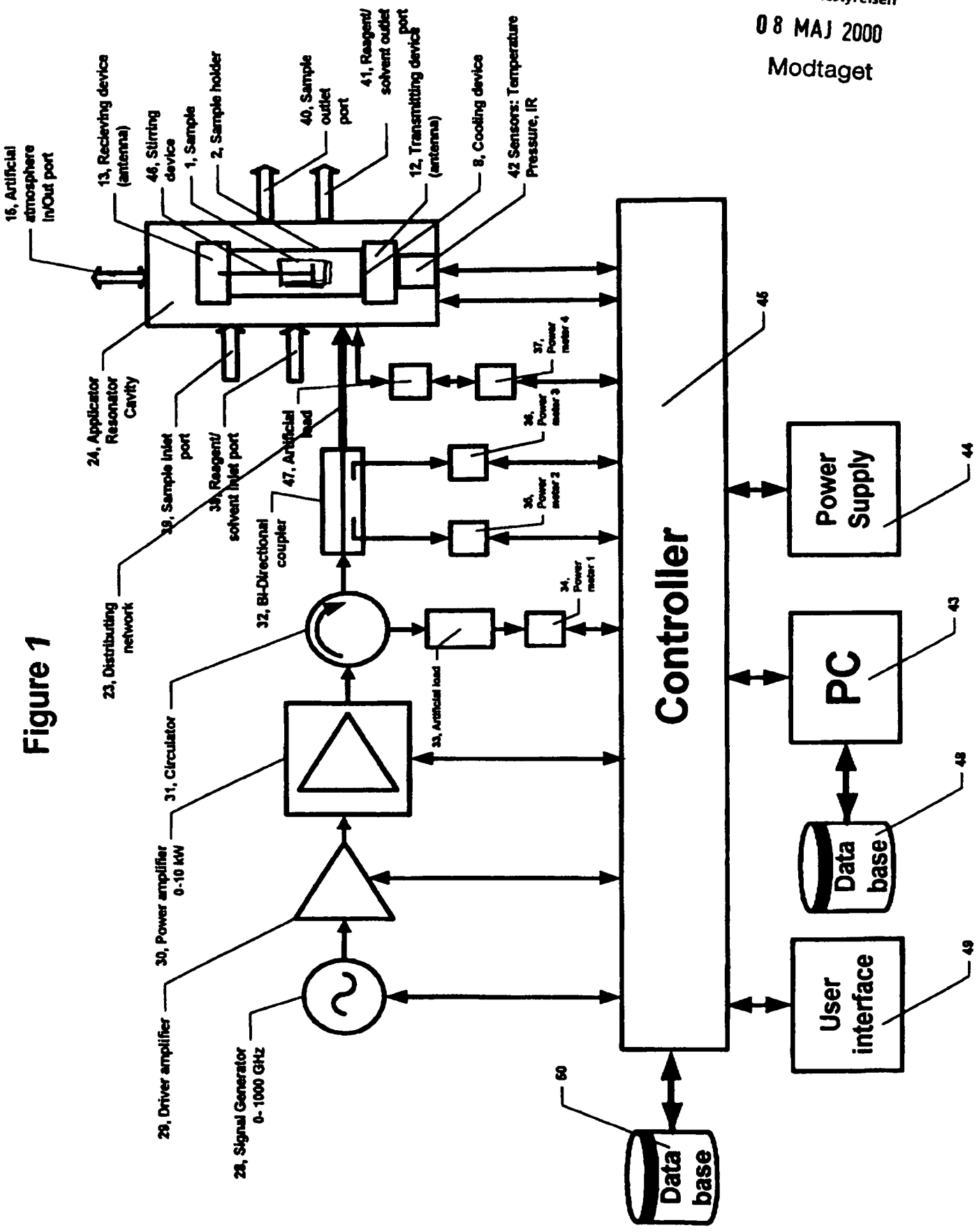


FIG. 2